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抑郁症患者工作记忆内情绪刺激加工的特点及其机制

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摘要 抑郁症患者在工作记忆内情绪刺激加工的特点为倾向于加工与负性心境一致的材料，被认为是抑郁症认知易感性的核心特征。目前研究者们围绕抑郁症工作记忆中央执行系统三个子功能的情绪刺激加工特点及其作用机制进行了大量研究，发现在更新功能上，患者难以移除负性情绪信息，且在正性信息的加工上存在缺损；在抑制功能上，患者难以抑制无关负性情绪信息进入工作记忆；在转换功能上，患者情绪材料转换困难的研究证据尚不充分。神经生理与脑成像的研究初步表明，工作记忆中的情绪刺激加工与抑郁症患者背外侧前额叶和前扣带回的功能激活水平异常有关。未来研究需评估工作记忆三个子功能对抑郁症状的差异性贡献及在情绪刺激加工上的统一性，并探究其随疾病发生发展变化的轨迹，谨慎选取并评估不同情绪刺激材料指标的诱发效应及其对工作记忆功能的独特影响。在此基础上，深入探究工作记忆内情绪刺激加工的神经机制，为工作记忆偏向矫正干预的临床应用及其预期效果提供理论依据和方向。

关键词 更新；抑制；转换；抑郁

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1 引言

抑郁症，又称重度抑郁障碍(major depressive disorder, MDD)，是最普遍的精神疾病之一。首次全国性精神障碍流行病学调查报告表明，中国重度抑郁障碍的终身患病率已达 3.4%，终生致残率超过 47%(Huang et al., 2019)。同时，抑郁症极高的自杀率和复发率，严重威胁到人类生命健康(Vos et al., 2015)，已成为世界范围内的首要致残原因(World Health Organization, 2017)。

抑郁症以持久的低落心境为主要临床特征，并伴随认知功能下降、自杀观念、睡眠障碍和明显的躯体症状等 (American Psychiatric Association, 2013)。其中，认知功能的改变不仅是抑郁症的典型症状，还是抑郁发作的重要风险因素(Mirza et al., 2016; Taylor & John, 2004)。Beck 的抑郁认知模型指出，这种对心境一致性负性情绪材料的优先加工，即认知偏向(cognitive bias)，在抑郁发作和维持中起着主导作用(Beck, 2008; Disner et al., 2011)。具体而言，在认知过程中过多地获取和加工负性信息会使个体对自我、日常生活和未来形成负性认知，最终导致个体陷入持久低落的情绪体验，处于抑郁状态。目前对于抑郁症的注意偏向(attention bias)、解释偏向(interpretation bias)和记忆偏向(memory bias)的研究相对充分(何振宏 等, 2015)，而且由此发展出了系统的认知偏向矫正(cognitive bias modification, CBM)干预方案，用于减轻抑郁症患者的认知偏向以及抑郁症状(Hoorelbeke & Koster, 2017; Koster & Hoorelbeke, 2015)。值得注意的是，这三种偏向均与工作记忆内负性情绪刺激加工能力的缺损存在密切相关。Joormann 和 Tanovic (2015)提出，对工作记忆内容的认知控制缺损与抑郁症患者的负性偏向有关，对工作记忆内负性信息的加工偏向使得患者难以主动采用适应性情绪调节策略，而更加偏好于使用非适应性的情绪调节策略。Lemoult 和 Gotlib(2019)则进一步指出，对工作记忆内负性信息加工的异常是抑郁症患者表现出注意偏向、解释偏向和记忆偏向的认知基础。可见，工作记忆内情绪材料的加工与抑郁症状的发生、发展和维持存在密切联系，并且可能是抑郁症认知易感性的核心表现。

工作记忆指对信息进行同时性存储和加工的容量有限的系统，是一般认知功能的核心系统和日常活动的基础(Baddeley, 2012; Baddeley & Hitch, 1974)。中央执行系统负责工作记忆中的控制性加工，并承担协调、监督语言回路和视空间画板两个子存储系统等重要

功能(Baddeley, 2012)。对抑郁症患者工作记忆存储功能的研究多采用的是中性材料，有研究表明抑郁症患者在言语工作记忆和视空间工作记忆上均存在损伤(Merriam et al., 1999; Zaremba et al., 2019)，也有研究发现抑郁症患者的言语与视空间工作记忆与健康对照组没有显著差异(Channon et al., 1993; Grant et al., 2001)。随着工作记忆理论和现代神经科学研究技术的发展，工作记忆的核心成分，即中央执行系统，日益受到研究者们的关注(Joormann et al., 2011; LeMoult & Gotlib, 2019; Levens & Gotlib, 2010)。早期研究多是将中央执行系统看作为单一结构的认知系统，但是这一过于宽泛的概念为中央执行系统的界定和测量带来了困难。认知控制（又称执行控制、执行功能），一般是指个体为了实现某个目标或者在完成复杂任务时，灵活地去调整和控制自己认知和行为的心理过程(Grahek et al., 2018; Shenhav et al., 2013)，因此认知控制常被用来描述所有复杂、高级认知活动的集合，例如双任务、计划、决策、工作记忆、认知灵活性等。Miyake(2000)采用潜变量建模的方法提出三成分模型的分离，推动了对认知控制的量化评估。更新(updating)、抑制(inhibition/inhibition control)与转换(shifting/switching)是认知控制最重要的三项子功能这一观点(Friedman & Miyake, 2017)在学界得到了广泛认可和运用 (Collette & Linden, 2002; 赵鑫, 周仁来，2011)。值得注意的是，三个子功能对应于三种不同的典型心理操作过程，同时也涉及一些共同的认知过程，如所有任务都涉及到对当前任务相关的目标或其他心理表征的动态存储和操作(Friedman & Miyake, 2017; Miyake et al., 2000)。三个认知控制子功能的统一性和分离性(unity and diversity)在脑损伤患者和健康人群中得到了进一步的证实和验证(Tsuchida & Fellows, 2013; 陈天勇, 李德明, 2005)。Baddeley (2012)指出了工作记忆中央执行系统分离的必要性，并且认为可参考认知控制的分离方式。目前工作记忆中央执行系统三个子功能的分离性已成为世界范围内研究工作记忆认知加工机制的经典研究视角(Karr et al., 2018)。抑郁症患者工作记忆中央执行系统不同子功能情绪加工的认知和神经机制是否存在显著差异，也是本综述关心的核心问题。

综述以往文献发现，先前大部分研究对抑郁症工作记忆更新和抑制功能的情绪加工特征进行了探讨，对转换功能研究较少，且研究结果并不一致，这使得抑郁症患者工作记忆情绪加工的内在机制并不明确，并为围绕工作记忆内负性刺激加工偏向开展认知偏向矫正训练带来了困难。因此，本文将围绕工作记忆中央执行系统不同子功能，从更新、抑制和转换三个方面对抑郁症患者工作记忆内情绪刺激加工的实证研究进行系统梳理, 进一步明晰抑郁症的情绪加工在不同工作记忆功能上的表现及其认知机制, 以揭示抑郁症工作记忆负性

情绪加工的核心特征，并对该领域研究有待回答的问题与发展动向进行讨论和展望。

2 抑郁症患者更新功能的情绪刺激加工特点

更新功能是指对工作记忆任务的监视和动态操作，以有效地匹配当前的任务要求(Joormann & Tanovic, 2015; Morris & Jones, 1990)。具体而言，由于工作记忆系统容量的有限性，个体需不断地用符合当前任务要求的新信息来替代无关的旧信息，对工作记忆中的存储对象加以调整和更改。当个体经历消极事件时，及时从工作记忆中移除消极的旧信息、纳入中性或积极的新信息，能帮助个体利用有限的认知资源进行适应性的情绪调节，减少负面信息的干扰。

2.1 行为学证据

移除是工作记忆更新功能的一个子过程(Ecker et al., 2014; Lewis-Peacock et al., 2018)。有研究表明，更新能力弱的个体难以移除工作记忆中的消极材料，导致对消极信息的反复加工，从而促进消极情绪的形成和维持(Pe et al., 2013)。Joormann 和 Gotlib(2008)编制了情绪 Sternberg 任务，将定向遗忘线索与经典的 Sternberg 再认识别任务相结合，以评估在工作记忆中移除无关信息的能力。该任务首先向被试同时呈现两组标记为红色或蓝色的情绪词汇；在线索阶段呈现一个红色(或蓝色)边框长方形，要求被试仅在工作记忆内存储标记为红色(或蓝色)的词语，并将蓝色(或红色)词移除出工作记忆；在探测阶段屏幕上出现一个词语，要求被试判断呈现的目标词汇是否来自与线索长方形颜色一致的词汇组，即相关词。采用该范式的研究发现，相比新出现的词汇，当探测词来自无关负性词汇组时抑郁症患者的反应时比健康对照组更长，而在正性词汇上则未发现组间差异(Joormann & Gotlib, 2008)。与诱发悲伤情绪状态的控制组或社交焦虑患者相比，抑郁症患者受负性信息的干扰最大(Joormann & Gotlib, 2008; Yoon et al., 2014)，表明抑郁症对工作记忆内负性信息的加工具有特异性，工作记忆更新时移除无关负性信息的困难是抑郁的重要认知易感性指标。

同时，也有研究者采用情绪 n-back 任务考察情绪效价对抑郁症患者工作记忆更新功能的影响。在采用情绪面孔(Everaert, Grahek, Duyck, et al., 2017; Levens & Gotlib, 2010)作为刺激材料的研究中，研究者要求被试判断当前出现刺激的情绪效价是否与 N 个试次前的目标刺激匹配。研究结果显示，相比正常个体，抑郁症患者更新负性刺激材料的反应时更长，更新正性刺激材料的反应时更短，提示抑郁症患者工作记忆中更新负性信息的速度减慢，而更新正性信息的速度过快。以缓解期抑郁症患者为对象的研究表明，在情绪 Sternberg 任务和

情绪 n-back 任务上，该群体也表现出移除正性刺激过快、更新负性刺激困难的行为模式(Levens & Gotlib, 2015; 刘明矾 等, 2015)，提示更新情绪刺激的困难是抑郁症的特质性而非状态性特征，会一直持续至抑郁症缓解期。

2.2 神经生理与脑影像证据

有研究指出，与正常个体表现出的对工作记忆内正性信息的优先加工不同(Cromheeke & Mueller, 2016; Pe et al., 2013)，抑郁症患者中缺乏正性优先效应(Goodin et al., 2019; Levens & Gotlib, 2009; Wante et al., 2018)。近来的一项 ERP 研究也为上述行为结果提供了神经生理的证据(Zhang et al., 2018)。该研究采用情绪词汇 n-back 范式发现，正性材料在抑郁症患者组中诱发的枕叶 P1 的波幅小于对照组，额叶 P2 和顶叶 LPP 成分波幅显著高于对照组，而负性材料仅诱发了波幅显著偏大的额叶 P2 和顶叶 LPP 波。N-back 任务所体现的更新可能涉及编码、匹配和维持三个认知过程，分布于枕叶的 P1 成分反映了对视觉刺激的早期加工，与刺激编码有关；而额区的 P2 反映了对刺激自上而下的认知控制，与刺激匹配这一过程密切相关；分布于顶叶的 LPP 则与记忆表征的维持密切相关。该研究提示抑郁症患者对积极信息早期编码加工的不足，对正性材料分配的认知资源较少；而在匹配和维持阶段，正性和负性情绪条件下均表现为 P2 和 LPP 波幅高于对照组，不受情绪效价的影响。这表明抑郁症患者工作记忆更新正性信息的功能不足与编码阶段的缺损密切相关。

脑影像研究表明，在维持负性情绪材料的记忆表征阶段，抑郁症患者左侧的背侧前扣带回(dorsal anterior cingulate cortex, dACC)激活水平低于健康对照组(Foland-Ross et al., 2013)。dACC 往往与认知控制功能有关(Dosenbach et al., 2007; Vincent et al., 2008)，提示抑郁症患者在存储负性刺激这一心境一致性材料时所需认知资源较少。值得注意的是，在情绪词汇 2-back 任务中，在更新情绪刺激时，抑郁症患者左侧 dACC 和背外侧前额叶(dorsolateral prefrontal cortex, dlPFC)激活水平高于正常群体，且 dACC 的激活程度与负性刺激条件下的反应时呈显著负相关(Gartner et al., 2018)，这提示 dACC 在工作记忆更新的不同加工阶段中可能扮演着不同的角色。可见，抑郁症患者在工作记忆内维持负性材料时所需认知资源较少，而在记忆更新阶段不断地将负性信息移除出工作记忆则需要付出更多的认知努力。另一方面，dlPFC 在工作记忆表征过程中起着重要作用，是执行控制的关键脑区(Chai et al., 2018; Demanet et al., 2016; Leon-Dominguez et al., 2015)。然而抑郁症患者需要付出更多的认知努力去保证与对照组一致的工作记忆任务表现，表现为 dlPFC 和 ACC 激活程度更高(Harvey et al., 2005)。对缓解期抑郁症患者的研究也证实，在负性面孔的干扰下进行 2-back 任务时，

dlPFC、腹外侧前额叶(ventrolateral prefrontal cortex, vlPFC)和眶额皮层的激活增强，而在正性面孔的干扰下，dlPFC、vlPFC 和腹侧纹状体的激活则减少，表现出了 dlPFC 和 vlPFC 的情绪效价特异性(Kerestes et al., 2012)。这表明相比正性面孔干扰，当抵抗负性面孔的干扰时，前额叶皮层需要调动更多认知资源来完成工作记忆任务。因此，结合 ERP 研究的结果，抑郁症患者工作记忆情绪加工的异常可能源于早期编码阶段对正性刺激加工不足，而在更新阶段移除负性刺激时需要付出更多的认知努力。

2.3 小结

以上的结果初步证实，抑郁症患者在工作记忆更新上的情绪加工特点，表现为负性情绪刺激加工偏向和正性情绪刺激加工效应缺失。负性情绪刺激加工偏向主要表现为抑郁症患者移除无关负性信息困难以及更新负性信息缓慢，这与更新负性信息时认知控制相关脑区(如 dlPFC 和 dACC)的过度激活有关。正性情绪刺激加工效应的缺失主要表现为抑郁症患者更新正性信息过快，这与早期阶段正性信息编码不足有关。此外，Zhang 等人(2018)采用情绪词汇的 2-back 任务没有发现抑郁症患者存在负性加工偏向，而采用情绪面孔的 2-back 任务(Everaert, Grahek, & Koster, 2017; Levens & Gotlib, 2010)以及采用情绪词汇的情绪 Sternberg 任务(Joormann & Gotlib, 2008; Yoon et al., 2014)的研究则发现抑郁症患者在记忆更新功能上表现出负性加工偏向，这提示工作记忆更新中的情绪信息加工会受到情绪刺激材料类型和实验范式的影响。

3 抑郁症患者抑制功能的情绪刺激加工特点

抑制功能或抑制控制是指个体抑制与任务无关信息进入工作记忆的能力(Diamond, 2013)。有效的抑制控制可以保护工作记忆中与任务相关的内容免受无关信息的干扰以及防止有限的工作记忆容量被无关信息占用(Getzmann et al., 2018)。抑郁症患者对无关负性信息进入工作记忆的抑制不足，致使工作记忆中相关的正性或中性信息受到干扰，阻碍个体从消极情绪中恢复(Dai & Feng, 2011b; Joormann et al., 2007)。

3.1 行为学证据

对情绪 Stroop 研究的元分析表明，与健康对照组相比，抑郁症患者受到更强的负性刺激干扰效应(Epp et al., 2012; Joyal et al., 2019)，且抑郁症状的严重程度越高，干扰效应越大(Epp et al., 2012)，证实抑郁症患者抑制负性刺激更困难。运用情绪 Go/No-go 范式的研究表明，在健康群体中，相比负性或中性刺激，正性刺激作为 Go 目标时的反应时更短(Erickson

et al., 2005; Hare et al., 2005)；而在抑郁症患者中，负性刺激作为 Go 目标时反应时更短(Erickson et al., 2005; Ladouceur et al., 2006; Murphy et al., 1999)。在 Go/No-go 范式中，Go 刺激的出现频率远高于 No-go 刺激，因此被试会形成对 Go 条件下刺激的优势反应。上述研究结果表明，相比正性刺激，抑郁症患者表现出对负性刺激的优势反应偏向。No-go 条件用于评估个体对优势反应偏向的抑制，与对照组相比，抑郁症患者 No-go 条件下对负性词汇的错误反应率更高(Erickson et al., 2005; Kyte et al., 2005)，提示抑郁症患者对负性信息的抑制存在困难。利用信号检测论方法进行分析也发现，当要求抑郁症患者对中性面孔做出反应并抑制对悲伤面孔的反应时，抑郁症患者的辨别率 d' 显著低于对照组，进一步说明抑郁症患者抑制负性信息的能力下降(Yu et al., 2017)。

3.2 神经生理与脑影像学证据

ERP 的研究也为先前的行为学发现提供了神经生理方面的证据。抑郁症患者情绪 Stroop 的干扰效应表现为枕叶 N1、P2 波幅小于对照组，而顶叶 N450 波幅则比对照组更负(Dai & Feng, 2011a)。负性刺激诱发的 N1 和 P2 的波幅减小，反映了在早期负性信息感知阶段需要的认知资源较少(Bernat et al., 2001)；N450 波幅的增加则反映了负性信息对注意的自动捕获(McNeely et al., 2008)。值得注意的是，Dai 等人的研究还发现缓解期抑郁症患者也表现出 N450 波幅的增加(Dai & Feng, 2011a)，说明抑制功能加工的负性偏向没有随着抑郁症状的改善而减弱，可能会一直持续至抑郁症缓解期。此外，在 Go/No-go 实验范式的 ERP 研究中，N2、P3 成分反映更高水平的认知阶段，并且两者在情绪冲突中表现出不同的功能，N2 与冲突监控有关，P3 与冲突解决和行为抑制有关(Kropotov et al., 2011; Monnart et al., 2016)。另一项使用情绪面孔作为 Go/No-go 刺激材料的研究发现抑郁症患者额叶 No-goN2 波幅较低，这与使用中性材料的 Go/No-go 研究结果一致(Bailey et al., 2014; Kaiser et al., 2003)，提示抑郁症患者的早期冲突监控能力受损；此外，有研究发现在悲伤面孔下患者额叶 No-goP3 波幅比对照组低，因此抑郁症患者对负性面孔反应抑制的选择性缺损还表现为晚期的冲突解决和行为抑制方面的缺损(Yu et al., 2017)。

脑成像研究发现，在认知任务中，与对照组相比，抑郁症患者额下回、dlPFC 和 vlPFC 激活减少(Chechko et al., 2013; Siegle et al., 2007; Wang et al., 2008)。这些脑区不仅与抑制控制有关，并且参与负性情绪的调节和重新评估(Ochsner et al., 2002; Ochsner et al., 2004)。因此，额叶网络功能的改变可能是抑郁症患者难以抑制负性刺激的神经基础。研究表明，抑郁症患者抑制负性情绪刺激的干扰时，dlPFC 的激活较低(Colich et al., 2016; Groenewold et al.,

2013)，内侧前扣带回(rostral anterior cingulate cortex, rACC)的激活增加(Eugene et al., 2010; Mitterschiffthaler et al., 2008)，而健康对照组则在抑制正性刺激的干扰时 rACC 激活增加(Eugène et al., 2010)。dlPFC 参与情绪冲突的监控，而 rACC 与情绪冲突的抑制有关(Etkin et al., 2006)，这说明抑郁症患者负性情绪冲突监控的能力受损，并且需要投入更多的认知资源对负性刺激引起的冲突进行抑制。此外，研究者发现在完成情绪 Stroop 任务时，负性干扰词在亚临床抑郁个体中诱发了更高水平的 dACC 和后扣带回(posterior cingulate cortex, PCC)激活，并且抑郁症状越严重，dACC 和 PCC 的功能连接(functional connectivity)越强(Kaiser et al., 2015)。功能连接是从功能整合的角度，刻画不同脑区信号的时间序列同步性(Biswal et al., 1995)。dACC 和 PCC 分别是额顶叶网络和默认网络的核心脑节点，这提示工作记忆内负性信息的抑制困难可能与脑网络间的异常连接有关。有研究指出，抑郁症患者的功能改变反映的不只是单一大脑区域的活动水平，还应关注功能网络水平上的改变(Hamilton et al., 2013)。静息态的 fMRI 研究也表明，抑郁症患者额顶叶网络和默认网络两个子网络间的连接要强于正常对照组(Sheline et al., 2010)，且抑郁症患者额顶叶网络内部及默认网络内部的连接模式也异于对照组(Yan et al., 2019; Zhao et al., 2019)。后续研究可结合工作记忆实验任务，考察任务态下抑郁症患者不同脑网络内部及脑网络间的功能连接及有向连接，尤其是额顶叶网络与默认网络时间序列信号上的因果关系，从而对抑郁症患者抑制功能受损的脑机制进行深入探索。

3.3 小结

以上的结果初步证实，抑郁症患者在工作记忆抑制功能上的情绪信息加工偏向，主要体现在对情绪信息的冲突监控缺损以及抑制负性信息困难，该特点与 dlPFC、ACC 的功能以及脑网络动态连接异常有关。采用任务态的研究发现抑郁症患者在抑制负性信息时，dlPFC 激活水平较低，而 rACC、PCC 等脑区则表现出过度激活(Colich et al., 2016; Kaiser et al., 2015; Mitterschiffthaler et al., 2008)。也就是说，当抑郁症患者对工作记忆中的负性情绪刺激进行识别和抑制控制时，自上而下的冲突监控与解决功能均存在缺损。此外，难以抑制负性刺激带来的干扰也可能与脑网络内和脑网络间的异常连接有关。脑网络异常功能连接模式的进一步明确可以为抑郁症的诊断与治疗提供神经影像学的生物标记物 (Hamilton et al., 2013)，因此仍需进一步明晰抑郁症患者脑功能的异常，进而对各个脑网络系统的动态连接进行探究。

4 抑郁症患者转换功能的情绪刺激加工特点

转换功能是指个体在工作记忆心理表征之间切换或不同任务之间重新分配认知资源的能力(Joormann & Tanovic, 2015)。良好的转换功能可以帮助个体在工作记忆中将注意焦点从与任务无关的消极情绪信息转移到任务相关的积极情绪信息上，从而采用适应性的情绪调节策略(Chun et al., 2011; Koster et al., 2013; Malooly et al., 2013)。

4.1 行为学证据

内部转换任务(Internal Shifting Task, IST)被广泛地运用于工作记忆转换功能的研究中。该任务最初由 Garavan 在 1998 年开发，后来研究者们将其改编为情绪转换任务(De Lissnyder, Koster, Everaert, et al., 2012; De Lissnyder, Koster, Goubert, et al., 2012; Everaert, Grahek, & Koster, 2017; Garavan, 1998)，任务要求被试分别对不同效价的情绪刺激进行心理计数。若当前试次刺激与前一试次刺激的情绪效价相同(如均为负性刺激)，则该试次为非转换试次；反之，则为情绪转换试次(如前一试次为负性刺激，当前试次为正性刺激)，通过计算转换试次与非转换试次的反应时差异来衡量转换代价，从而评估情绪刺激对个体转换功能的影响。目前的实证研究多是比较中性刺激间的转换代价和情绪刺激间的转换代价的差异，没有对情绪效价的偏向性进行探讨。如 De Lissnyder、Koster 和 Everaert 等人(2012)探讨了中性条件下(对性别类别计数)与情绪条件下(对中性和负性面孔计数)的转换困难，结果表明抑郁症患者在中性和情绪条件的转换代价均高于正常个体，并未表现出情绪的特异性，提示抑郁症患者在切换工作记忆中的心理表征时表现出普遍的转换功能障碍。目前也有部分研究支持抑郁症患者中存在情绪转换困难(Lo & Allen, 2011; Lo & Liu, 2017)，具体而言，在中性词汇条件下，抑郁症患者与正常个体的转换代价没有显著差异；在正性和负性词汇之间进行切换的情绪条件下，则表现为抑郁症患者的转换代价显著高于正常个体，并且抑郁症状得分与情绪条件下的转换代价呈显著正相关(Lo & Allen, 2011)。值得注意的是，对亚临床抑郁个体的研究则提示情绪转换困难可能存在年龄差异，青少年亚临床抑郁人群表现出高于对照组的情绪转换困难(Wante et al., 2017)，而成年亚临床抑郁人群则没有表现出显著的转换障碍(De Lissnyder, Koster, & De Raedt, 2012)。

4.2 神经生理与脑影像学证据

目前，尚未有针对性的研究考察抑郁症患者转换功能情绪刺激加工的神经机制。以心境障碍患者为对象的研究发现，在完成情感转换任务时，相比正常对照组，患者的情绪转换代价更高。fMRI 的结果显示，患者的额下回、左侧楔前叶、顶内沟和 ACC 的膝下部的激活水平显著高于正常对照组，提示心境障碍患者表现出的情绪转换困难与额顶叶网络的过度激活有关(Piguet et al., 2016)。但是该研究中仅有 9 例抑郁症患者，关于抑郁症患者转换功能的神经机制，尤其是情绪转换困难和额顶叶网络功能异常的关系，有待进一步探讨。

4.3 小结

综上，围绕抑郁症患者工作记忆转换中情绪信息加工的研究相对较少，而且在不同人群中的研究结果并不一致。研究者推测该不一致可能与两个影响因素有关，一方面，可能与选用刺激材料的效价有关。如在正性词汇和负性词汇之间的转换代价表现为抑郁症患者显著高于正常个体(Lo & Allen, 2011)。而在愤怒面孔和中性面孔之间的转换中，抑郁症患者不受情绪材料的影响，仅表现出一般的转换功能障碍(De Lissnyder, Koster, Everaert, et al., 2012)。这可能是因为中性面孔在抑郁群体中更容易被知觉为具有威胁性(Bertocci et al., 2012; Tavitian et al., 2014)，故在两者间的转换没有出现偏向。另一方面，可能受到其他一些疾病相关变量的调节，如思维反刍水平。思维反刍是指个体对负性事件相关的情绪体验、起因和后果进行反复思考的思维倾向(Koster et al., 2011; Nolen-Hoeksema & Morrow, 1991)。使用 IST 范式的研究结果表明，情绪刺激转换困难与反刍水平有关(Chen et al., 2016; De Lissnyder, Koster, Everaert, et al., 2012; De Lissnyder, Koster, Goubert, et al., 2012)，尤其是在负性刺激下(Koster et al., 2013)。一项前瞻性研究发现，在缓解期抑郁症患者中，情绪条件下的转换代价可以预测个体一年后抑郁症状的严重程度，且思维反刍在转换代价与抑郁症状之间起完全中介作用(Demeyer et al., 2012)。因此，未来研究还需进一步探讨可能造成混淆的相关因素。此外，对转换功能情绪加工背后脑机制的探讨也亟需研究者的关注。

5 总结与展望

5.1 总结

综上可以发现，抑郁症患者工作记忆内情绪信息加工表现出负性情绪刺激加工偏向，即工作记忆偏向(working memory bias)，体现为以下三种模式：(1)抑郁症患者有负性偏向，健康对照组有正性偏向(Erickson et al., 2005; Kyte et al., 2005; Levens & Gotlib, 2010)；(2)抑郁症患者有负性偏向，健康对照组无偏向(Dai & Feng, 2011a; Joormann & Gotlib, 2008; Joyal et al., 2019; Mitterschiffthaler et al., 2008; Yu et al., 2017)；(3)抑郁症患者无偏向，健康对照组有正性偏向(Wante et al., 2018; Zhang et al., 2018)。但总体来看，抑郁症患者的情绪刺激加工偏向在工作记忆三个子功能上均有所体现，并且在更新功能上的负性偏向持续至缓解期。具体而言，抑郁症患者在更新功能上难以及时移除工作记忆中的负性情绪信息以及对正性信息编码存在缺损，在抑制功能上难以抑制无关负性情绪信息进入工作记忆，在转换功能上的情绪刺激加工偏向的研究证据仍待加强。

对工作记忆情绪刺激加工的讨论为认知偏向研究提供了新视角，厘清抑郁症患者在工作

记忆层面上的情绪刺激加工的特点及其核心作用机制，有助于进一步揭示抑郁症认知偏向的内在机制，推动对抑郁症发病与疾病维持机制的关注和探讨，是对抑郁认知模型的拓展和加深。在最近发表的一项综述中，Joormann 指出，对人类高级认知加工过程的基础性研究已取得较大进展，将其整合到对抑郁症特异性情绪加工过程和情绪调节障碍的临床研究中，是推动认识与抑郁症病因和疾病发展密切相关的认知易感因素的重要途径，同时有助于设计靶向抑郁症患者认知偏向的精准干预方案，并为其效果的验证和评估提供科学依据(Joormann, 2018)

5. 2 未来研究展望

如前文所述，虽然目前抑郁症工作记忆内情绪刺激加工的行为和神经机制研究已经取得一些成果，但仍有一些科学问题需要继续探讨，未来的研究可以从以下几个方面加以关注。

第一，评估不同工作记忆偏向对抑郁症状的差异性贡献。有研究者提出，抑郁症认知偏向的现有研究受限于单个特定的信息加工阶段，使得对不同的认知过程之间的相互作用及其对抑郁症状的影响所知甚少(Everaert et al., 2014)。在诸多认知过程中，注意与工作记忆的关系最为密切。以往有研究提出，注意是工作记忆的守门人(gatekeeper)，工作记忆又会引导和调控注意选择过程(Awh et al., 2006; Soto et al., 2012)。研究表明抑郁症患者注意偏向的核心特征是对负性刺激的加工偏向以及注意解除困难，对正性刺激注意减少(何振宏 等, 2015)。目前的多数研究还停留在对抑郁症注意偏向、工作记忆偏向等认知偏向的认知加工过程和神经机制的探讨上，对抑郁症不同认知功能上负性偏向间关系的实证研究较少。值得注意的是，近年来研究者提出了联合认知偏向假说(the combined cognitive bias hypothesis)，试图整合抑郁症不同认知偏向间的关系。联合认知偏向假说认为，抑郁症状的发生机制存在多个因果链，每种认知偏向并不是孤立存在的，而是存在相互影响和相互作用(Everaert et al., 2020; Everaert et al., 2012)。具体而言，抑郁症患者对负性刺激的注意偏向会导致进入工作记忆内的负性信息增多，使得工作记忆内情绪刺激加工困难，从而影响长时记忆中情绪信息的编码和提取，促进并加重抑郁症患者的记忆偏向(Everaert et al., 2020)。但该假说仍需实证研究数据的验证，不同认知偏向对抑郁症状的特异性贡献值得研究者在未来加以关注 (Marchetti et al., 2018)。工作记忆三个子功能和不同的认知偏向在抑郁症状的产生中又是如何起作用？目前仅有一项研究对此进行了初步探索。Everaert, Grahek 和 Koster(2017)发现转换功能和更新功能的情绪加工偏向通过解释偏向对抑郁症状的严重程度产生间接影响，抑制功能的情绪加工偏向则通过注意偏向和解释偏向对抑郁症状产生间接影响，初步显示了三个子功能对抑郁

症状作用机制的差异性。同时，有研究表明抑郁症患者在感觉记忆阶段也存在情绪加工缺损，表现出负性加工偏向(Chang et al., 2010；Zhang et al., 2016)。抑郁症对负性情绪刺激自下而上的情绪加工增强，与杏仁核和梭状回等脑区的过度激活有关(廖成菊，冯正直，2010)。对抑郁症情绪加工与不同认知加工成分交互的特点的探讨将有助于进一步揭示抑郁症患者情绪和认知易感性的内在作用机制(Dolcos et al., 2020)。

此外，工作记忆内负性刺激加工偏向还被认为是抑郁症情绪调节障碍的潜在认知基础(Joormann & D'Avanzato, 2010; Joormann & Tanovic, 2015)，负性偏向越严重的个体更倾向于采用非适应性的情绪调节策略(如思维反刍)，更少采用适应性的情绪调节策略(如认知重评)，进而加剧负性情绪体验的维持(Cohen et al., 2015; Pe et al., 2013)。目前研究发现转换功能上的负性偏向会通过思维反刍对抑郁症状产生影响(Demeyer et al., 2012)，其他两个子功能通过情绪调节策略影响抑郁症状的作用机制仍待补充。未来研究需要考察工作记忆三个子功能之间是如何相互影响，并检验三个子功能通过其他认知偏向和情绪调节策略对抑郁症核心症状的独特作用路径，以更深刻地揭示抑郁症患者工作记忆内情绪刺激加工的潜在机制。

第二，探讨工作记忆三个子功能间的联系。目前抑郁症患者工作记忆情绪刺激加工的研究主要集中在更新和抑制方面，对转换功能的研究比较少，仍需进一步的研究去揭示抑郁症工作记忆转换中情绪信息加工的特点及其内在机制。值得注意的是，大多数研究仅单独考虑抑郁症在工作记忆单个子功能上的情绪加工特点，从功能分离的角度来探讨单个子功能的认知和神经加工特点及其影响因素。工作记忆中央执行系统三个子功能的内在联系也一直备受关注，三个子功能存在一些共同的认知过程，均涉及对工作记忆心理表征的动态存储和操作(Friedman & Miyake, 2017; Miyake et al., 2000)。对正常人群工作记忆脑功能影像的元分析也表明，三个子功能的脑激活模式存在较大重叠(Nee et al., 2013; Niendam et al., 2012)。从目前的研究结果来看，三个子功能在抑郁症工作记忆情绪加工上体现出分离性，支持中央执行系统的可分离性。对于工作记忆三个子功能在情绪加工上的统一性和分离性在抑郁症患者中的表现，仍需在同一项研究中同时考察抑郁症患者在这三个成分上的加工特点，并采用潜变量建模或其他量化方法进行验证。

第三，关注高危人群，探究工作记忆偏向的发展变化轨迹。目前的研究发现，更新功能的情绪刺激加工偏向在亚临床抑郁、抑郁发作期及缓解期的模式是一致的。而抑制功能则存在不一致的结果，有的研究表明缓解期患者表现出与抑郁症患者一致的负性加工偏向(Dai & Feng, 2011a; Joormann & Gotlib, 2010)，有的研究未发现缓解期患者与正常个体在行为表现

上存在差异(Goeleven et al., 2006; Joormann, 2004)，为工作记忆不同子功能的加工特点随疾病病程表现出特异性提供了初步的证据。以亚临床抑郁群体或缓解期患者为研究对象，还能减少药物副作用等干扰因素的影响(Ahern & Semkovska, 2017)。扩大研究群体以探究工作记忆偏向随症状发展的变化轨迹，可以有利于分离出状态性、特质性及复发相关的认知易感性特征，进一步明确不同工作记忆子功能上的情绪信息加工在抑郁症状产生和维持中的差异性贡献。

第四，刺激材料在编码方式和唤醒度上的差异对工作记忆加工过程的作用机制上可能存在根本性不同，需谨慎选取并评估不同情绪刺激材料指标的诱发效应及其对工作记忆功能的影响。现有研究采用的刺激材料主要是情绪词汇和情绪面孔。目前研究显示，在评估抑郁症工作记忆偏向上，情绪面孔比情绪词汇更为灵敏(Gartner et al., 2018; Levens & Gotlib, 2010; Zhang et al., 2018)。而相比情绪面孔，场景图片的情绪凸显性更强, 诱发的情绪体验更贴近真实生活。最近的研究指出，相比感知特征加工的情绪面孔和情绪场景图片，基于语义知识加工的情绪词汇所引发的唤醒水平更低，情绪效应更弱(Yuan et al., 2019; 王霞 等, 2019)。未来研究可以通过控制三种材料的情绪属性(如效价、唤醒度等)，以评估不同情绪刺激材料在抑郁症患者中的情绪诱发效应。此外，在情绪加工偏向的研究中，应选取何种负性情绪刺激材料也存在争议。有研究者认为抑郁症患者对悲伤情绪更敏感，选用悲伤面孔作为刺激材料唤醒度更高，也更符合抑郁症患者的真实情况(Gollan et al., 2008)。也有研究者认为愤怒刺激材料引发的社会拒绝体验，更能增加抑郁症患者的自我相关性(Tavitian et al., 2014)，但暂未有研究比较悲伤和愤怒两种负性材料对抑郁症患者工作记忆加工的影响。因此，厘清情绪材料类型和唤醒度等因素的影响，并考察不同负性情绪材料影响工作记忆加工的潜在机制，对解决当前研究结果的不一致也具有重要的实践意义。

第五，目前关于抑郁症工作记忆偏向的神经机制研究处于发展萌芽阶段，亟需更多实证研究的补充和加强。研究初步显示，在更新负性情绪刺激时，抑郁症患者左侧 dACC 和 dlPFC 激活水平高于正常群体；抑郁症患者抑制负性情绪刺激的干扰时，rACC 的激活较高，而 dlPFC 的激活较低。已有研究指出 dACC 与 rACC 在情绪加工中的功能分离，前者与负性情绪心理表征的加工和评估有关，后者则参与自上而下的负性情绪抑制过程(Etkin et al., 2011)。因此，抑郁症患者所表现出的情绪调节障碍可能源于个体在情绪心理表征加工和评估方面的功能缺损，且在进行情绪调节以减少消极情绪体验时无法有效地抑制负性材料的影响。目前研究还显示抑郁症患者 dlPFC 的激活模式在更新功能和抑制功能上表现不同，可能是因为

脑影像研究多采用 n-back 任务考察工作记忆更新的脑机制，有的研究认为 n-back 任务同时涉及匹配、移除等多个心理加工过程(Chen et al., 2008)，难以有效地反映工作记忆能力的个体差异(Jaeggi et al., 2010)，对 n-back 任务用于评估工作记忆功能的有效性提出了质疑。因此，不同工作记忆子功能情绪加工特点的神经机制及其之间的差异仍待探讨。此外，研究结果的可重复性也是一个重要问题。对抑郁症患者神经影像学数据的元分析指出，目前研究中报告的抑郁症患者在认知与情绪加工的任务与正常对照组脑激活模式的不一致，在很大程度上源于抑郁症疾病本身的复杂性、样本量的大小以及统计分析方法的差异等，仍需增加高可重复性的研究以得出更可信的推论(Muller et al., 2017; Wang et al., 2015)。有研究者提出可通过在神经影像学研究中设置标准化的实验流程(如成套测验和成像协议)以减少样本特征和研究方法所带来的变异，提高研究结果的可验证性和临床应用价值(Korgaonkar et al., 2013; Zuo et al., 2019)。

最后，应围绕抑郁症患者工作记忆偏向开展靶向性的工作记忆训练, 考察工作记忆加工中的负性偏向和抑郁症状的动态依存关系和影响路径, 为认知偏向与抑郁症的因果关系提供直接证据。已有研究表明，工作记忆训练能有效降低个体的抑郁易感性，提高情绪调节能力(Beloe & Derakshan, 2019; 彭婉晴 等, 2019)。情绪工作记忆训练指在工作记忆任务中采用情绪图片、情绪词汇、情绪面孔等情绪性材料的训练范式，已有研究探讨了情绪工作记忆训练在健康人群(Schweizer et al., 2011; 潘东旎 等, 2018)以及抑郁症患者中(Iacoviello & Charney, 2015)的潜在效益及其机制。Schweizer 等人(2011)比较了中性与情绪工作记忆训练方案的有效性，发现使用负性面孔和负性词汇的双 n-back 任务提高了健康人群在情绪 Stroop 任务中的表现。八次的情绪面孔 n-back 训练可减轻抑郁症患者的抑郁症状(Iacoviello & Charney, 2015)，然而，也有一些研究发现工作记忆训练在缓解抑郁情绪上的作用非常有限(de Voogd et al., 2016; Onraedt & Koster, 2014; Wanmaker et al., 2015)。最近有研究者设计了工作记忆偏向矫正任务(working memory bias modification task)，训练个体在工作记忆编码阶段移除负性词汇，保留积极词汇和中性词汇，从而达到矫正工作记忆内负性刺激加工偏向的效果。该研究发现训练能提升高反刍思维个体在前摄干扰任务中的成绩，表现为训练组个体训练后受负性词的干扰降低(Robinaugh et al., 2016)。但该训练仅进行了一次，并未考察训练效应的维持，而且也未设置迁移任务。未来研究仍需寻求更多的证据去考察训练增益的内在机制，进一步厘清工作记忆内情绪刺激加工与抑郁症之间的关系，并设计出更具有靶向性和应用价值的干预训练。

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Processing of emotional information in working memory in Major Depressive Disorder

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Abstract: Major Depressive Disorder (MDD) is associated with mood-congruent processing biases towards negative information in working memory (WM), which is considered as the core manifest of cognitive vulnerability of MDD. This review provides an overview of the biased processing of emotional information of depression in three executive components of WM. Patients with MDD have difficulties in disengaging from negative information and present insufficient processing of positive materials during WM updating. MDD patients also exhibit impairments in suppressing irrelevant negative information and cannot effectively prevent the irrelevant negative information entering WM during inhibition. The findings of emotion-specific dysfunctions of shifting function in depression are inconsistent. Electrophysiological and neuroimaging studies suggest that the biased processing in WM is associated with altered brain activations in dorsolateral prefrontal cortex and anterior cingulate cortex. Future research is needed to investigate the different contribution of each type of biased processing to depressive symptoms, the unity of the biased processing in three WM components, the impact of biased processing in different stages of MDD, and the induction effects of different emotional materials on biased processing. Moreover, unraveling the neurophysiological mechanisms underlying the process of emotional materials in WM could help resolve the inconsistency of previous findings and benefit future development of cognitive bias modification interventions for biased processing in WM of depression.

Key words: updating; inhibition; shifting; depression